REMARKS

After entry of this amendment, claims 17-56 are pending. Claims 1-16 were canceled. Claims 17-56 are new. Support for new claims 17-56 can be found in the claims as originally filed and throughout the specification.

Support for "immunoglobulin light chain transgene construct that encodes V, J and constant regions" language in new claim 17 can be found, for example, at page 44, lines 28-36; support for "sequences operably linked to transcription regulatory sequences" language can be found, for example, at page 32, lines 11-16 and at page 45 lines 15-22; support for "*in vivo* rearrangement" language can be found, for example, at page 7, lines 29-30; support for "integration in nonhuman animal" language can be found, for example, and at page 6, lines 12-14; support for "producing a rearranged gene encoding a human light chain polypeptide" language can be found, for example, at page 33, lines 9-14; support for the V_κ segment, J_κ segment , C_κ segment and human 3' kappa enhancer language can be found, for example, at page 111, lines 35-39 and in the Examples at page 53, lines 11-17. Further support can be found in the Examples at page 174, lines 22-31.

Support for new claim 18 can be found, for example, at page 174, lines 22-27.

Support for new claim 19 can be found, for example, at page 6, lines 12-14; at page 33, lines 9-37; and at page 88, line 29 through page 89, line 4.

Support for new claim 20 can be found, for example, at page 6, lines 11-25.

Support for new claim 21 can be found, for example, at page 8, lines 15-19; at page 33, lines 9-13.

Support for new claim 22-26 can be found, for example, at page 7, lines 29-34; and at page 33, lines 9-13.

Support for new claim 27 can be found, for example, at page 46, lines 31-34.

Support for new claim 28 can be found, for example, at page 7, lines 17-21.

Support for new claim 29 can be found, for example, at page 6, lines 12-16.

Support for new claim 30 can be found, for example, at page 6, lines 12-16; page 7, lines 22-28; and at page 32, lines 20-26.

Support for new claim 31 can be found, for example, at page 6, lines 12-16; and at page 32, lines 20-26.

Support for new claim 32 can be found, for example, at page 10, lines 5-8; and at page 43, lines 14-16.

Support for new claim 33 can be found, for example, at page 7, lines 13-17. Additional support can be found, for example, at page 7, lines 22-28 and at page 161, lines 24-32.

Support for new claim 34 can be found, for example, at page 29, lines 19-25 and at page 61, lines 33-38.

Support for new claim 35 can be found, for example, at page 7, lines 26-28.

Support for new claim 36 can be found, for example, at page 163, line 37 through page 164, line 3.

Suppor for new claim 37 can be found, for example, at page 248, lines 9-28.

Support for new claim 38 can be found, for example, at page 163, lines 9-27.

Support for new claim 39 can be found, for example, at page 41, lines 4-9.

Support for new claim 40, can be found, for example, at page 162, lines 11-19.

Support for new claim 41, can be found, for example, at page 46, lines 31-34. Further support can be found at page 163, lines 37 through page 164, line 3 and at page 164, lines 9-27.

Support for new claim 42, can be found, for example, at page 46, lines 31-43. Further support can be found at page 91, lines 8-10 and at page 164, lines 9-27.

Support for new claim 43, can be found, for example, at page 61, lines 27-32.

Support for new claim 44, can be found, for example, at page 31, lines 25-33.

Support for new claim 45, can be found, for example, at page 43, lines 17-34 and at page 44, lines 10-17.

Support for new claim 46, can be found, for example, at page 43, lines 17-34 and at page 44, lines 10-17.

Support for new claim 47, can be found, for example, at page 15, lines 29-37.

Support for new claim 48 and 49, can be found, for example, at page 61, lines 21-26.

Support for new claim 50 and 51, can be found, for example, at page 61, lines 33-38.

Support for new claim 52, can be found, for example, at page 9, lines 29

Support for new claim 53, can be found, for example, at page 45, lines 15-22.

Support for new claim 54, can be found, for example, at page 44, lines 10-17.

Support for new claim 55, can be found, for example, at page 55, lines 18-22.

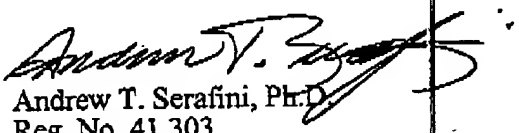
Support for new claim 56, can be found, for example, at page 55, 18-22 and page 61, lines 33-38.

CONCLUSION

With entry of this Preliminary Amendment, claims 17-56 are pending in the application. Also, the specification has been amended to insert a reference to the priority applications. No new matter has been introduced.

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 650-326-2400 X5228.

Respectfully submitted,



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Appendix: Pending claims with entry of this amendment

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

--17. An immunoglobulin (Ig) light chain transgene construct comprising DNA sequences that encode human variable (V), joining (J) and constant regions of a human Ig protein, which sequences are operably linked to transcription regulatory sequences and capable ofundergoing gene rearrangement in vivo, when integrated in a non-human transgenic animal, to produce a rearranged gene encoding a human light chain polypeptide, the construct further comprising at least one human Vκ segment, at least one Jk segment, at least one human Ck segment, and a human 3' kappa enhancer segment.

18. The construct of claim 17, wherein the human 3' kappa enhancer segment is a 4 kb BamHI fragment containing the human 3' kappa enhancer.

19. A transgenic nonhuman mammal comprising the transgene of claim 1.

20. The transgenic nonhuman mammal of claim 19, wherein the transgene is expressed in B cells of the transgenic nonhuman mammal.

21. The transgenic nonhuman mammal of claim 19, wherein the transgene is in the germline of the transgenic non-human mammal.

22. The transgenic nonhuman mammal of claim 19, further comprising an Ig heavy chain transgene construct.

23. The transgenic nonhuman mammal of claim 21, wherein the transgene is rearranged.

24. The transgenic nonhuman mammal of claim 21, wherein the transgene is unrearranged.

25. The transgenic nonhuman mammal of claim 22, wherein the transgene is rearranged.

26. The transgenic nonhuman mammal of claim 22, wherein the transgene is unrearranged.

27. The transgenic nonhuman mammal of claim 19, wherein the mammal makes an antibody response following immunization with an antigen.

28. The transgenic nonhuman mammal of claim 27, wherein the antigen is a human antigen.

29. The transgenic nonhuman mammal of claim 27, wherein the antibody response comprises a population of antibodies which comprise human μ chain-containing immunoglobulins and human γ chain-containing immunoglobulins.

30. The transgenic nonhuman mammal of claim 20, wherein the B cells produce a heterologous antibody.

31. The transgenic nonhuman mammal of claim 30, wherein the B cells produce a population of heterologous antibodies of more than one isotype.

32. The transgenic nonhuman mammal of claim 19 wherein the nonhuman mammal is a rodent.

33. A method for generating a plurality of B cells expressing human antibody sequences, the method comprising:

providing a transgenic nonhuman mammal of claim 19; and

immunizing the transgenic nonhuman mammal to generate B cells producing a population of heterologous antibodies.

34. The method of claim 33, further comprising collecting the B cells producing a population of heterologous antibodies.

35. The method of claim 34, further comprising fusing the B cells producing a population of heterologous antibodies with immortalized cells to form hybridomas.

36. The method of claim 35 further comprising collecting the human antibody sequences from the hybridomas.

37. The method of claim 36, wherein the human antibody sequences are purified.

38. The method of claim 33, further comprising collecting the sequences encoding human antibodies.

39. The method of claim 38, wherein the sequences encoding human antibodies are full length.

40. The method of claim 39, further comprising expressing the sequences in a transfected cell.

41. A method of generating antigen-specific hybridomas secreting human sequence antibody, the method comprising:

immunizing the transgenic nonhuman mammal of claim 19 with a predetermined antigen;

fusing lymphocytes from the transgenic mouse with immortalized cells to form hybridoma cells; and

determining the binding of the antibody produced by the hybridoma cells to the predetermined antigen.

42. A method for generating a human sequence antibody that binds to a predetermined antigen, the method comprising the following steps:

immunizing the transgenic nonhuman mammal of claim 19 with a predetermined antigen; and

screening hybridoma cells formed for the presence of antigen reactive antibodies.

43. The method of claim 42, wherein the antigen reactive antibodies are secreted from the hybridoma in culture.

44. The method of claim 42, wherein the antigen reactive antibodies are substantially pure.

45. A method for producing rearranged immunoglobulin sequences comprising:

providing the transgenic nonhuman mammal of claim 19;

obtaining the rearranged immunoglobulin sequences from the transgenic nonhuman mammal.

46. The method of claim 45, wherein the obtaining step comprises collecting B cell lymphocytes containing the rearranged immunoglobulin sequences from the transgenic nonhuman mammal.

47. The method of claim 46, wherein the obtaining step comprises isolating and amplifying mRNA from B cell lymphocytes to generate cDNA.

48. The method of claim 47, further comprising isolating and amplifying heavy and light chain variable region sequences from the cDNA.

49. An isolated nucleic acid encoding the heavy and light chain variable region sequences of claim 48.

50. An isolated nucleic acid encoding the heavy chain variable region sequences of claim 48.

51. An isolated nucleic acid encoding the light chain variable region sequences of claim 48.

52. A vector comprising the nucleic acid of claim 49.

53. An expression vector comprising the nucleic acid of claim 49 in which the heavy and light chain variable regions sequences of the nucleic acid are operatively linked with a regulatory sequence that controls expression of the nucleic acid in a host cell.

54. A host cell comprising the nucleic acid of claim 49, or progeny of the cell.

55. The host cell of claim 54 which is a eukaryote.

56. The method of claim 45, further comprising:

culturing the host cell of claim 54 under conditions such that the nucleic acid is expressed; and

recovering the nucleic acid from the cultured host cell or its cultured medium.–